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Peripheral blood mono-nuclear cells derived from Alzheimer's disease patients show elevated baseline levels of secreted cytokines but resist stimulation with β-amyloid peptide

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ABSTRACT

Objectives: Among several other factors, the neuro-toxic β-amyloid peptide (βAP)-induced inflammatory mechanisms have also been implicated in the pathogenesis of Alzheimer's dementia (AD). Cytokines have recently emerged as prime candidates underlying this immune reaction. The purpose of this study was to evaluate the inflammatory response of peripheral blood mono-nuclear cells (PBMC) in AD.
Design: Cross-sectional (observational) study.
Setting: Behavioral and cognitive neurology clinic of the *Universidade Federal de Minas Gerais* in Belo Horizonte, Brazil.
Participants: AD patients (n = 19), healthy elderly (n = 19) and young (n = 14) individuals.
Measurements: Cytokine levels were assessed by enzyme-linked immuno-sorbent assay (ELISA) after exposing cells to a broad range of βAP concentrations (10^{-4}–10^{-10} M) as a stimulus. AD samples were weighed against leukocytes harvested from non-demented young and elderly subjects.
Results: Cytokine production of PBMCs in the youth was characterized by low baseline levels when compared to cells from the older generation. In the aging population, AD cells were distinguished from the healthy elderly sub-group by an even higher basal cytokine secretion. The low resting concentration in young individuals was markedly increased after treatment with βAP, however cells from the elderly, irrespective of their disease status, showed unchanged cytokine release following βAP administration. Non-specific activation of PBMCs with anti-CD3/CD28 antibodies resulted in elevated interleukin (IL)-1β concentrations in AD.
Conclusions: These results demonstrate a general over-production of cytokines and resistance to βAP in the old comparison group, with a more pronounced disruption/boosted pattern in AD. Our findings are in line with the hypothesis of "inflammaging", *i.e.* an enhanced inflammatory profile with normal aging and a further perturbed environment in AD. The observed cytokine profiles may serve as diagnostic biomarkers in dementia.

Introduction

Alzheimer's disease (AD) is a neuro-degenerative disorder characterized by progressive loss of cognitive functions, especially memory (Alzheimer's Association, 2009). The main histo-pathological picture consists of neuronal loss in selected brain regions, as well as deposition

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